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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,523	03/12/2009	Frederick John Rowell	5585-76118-01	4714

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EXAMINER	
GAKH, YELENA G	

ART UNIT	PAPER NUMBER
1777	

NOTIFICATION DATE	DELIVERY MODE
12/20/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/585,523	ROWELL ET AL.	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1777	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1, 6-21, 23-27 and 29-30* is/are pending in the application.

5a) Of the above claim(s) *27,29 and 30* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,6-21 and 23-26* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☒ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *07 July 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/07/06, 03/12/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Election of Invention I, claims 1-19 and 23-26 and amendment filed on 10/27/11 are acknowledged. Claims 2-5, 20-22 and 28 are cancelled. Claims 1, 6-21, 23-27 and 29-30 are pending in the application. Claims 27, 29 and 30 are supposed to be cancelled or indicated as withdrawn, as directed to the non-elected invention. Claims 1, 6-21 and 23-26 are considered on merits.

Drawings

2. The drawings are objected to because, first, the drawing does not have the proper notification, such as "Figure 1a-c". Second, the photograph 1c is totally black. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

3. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without

underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to because it does not comprise disclosure which is detailed enough for practicing the invention by a routineer in the art. The drawings are not described. The preparation of the particles is not provided. The specification discloses only encapsulation of the marked biomolecules in sol-gel matrix, which converts into solid xerogel upon removing the solvent. No disclosure of forming nanoparticles from such matrix is provided in the specification.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 6-17, 19-21 and 23-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recite "a nanoparticle, which encapsulates a fluorescent material". The specification does not provide any disclosure for forming nanoparticles out of sol-gel which encapsulates fluorescently tagged biomolecules. The specification mentions encapsulation only in two paragraphs:

> "[0013] Sol gels' processing generally comprises the formation of a dual phase material of a solid polymer matrix skeleton filled with a solvent through a sol gel transition. When the solvent is removed, the gel converts to a xerogel. Sol gels have been widely used as matrices in a variety of analytical systems, including for encapsulation of biological macromolecules such as proteins and enzymes or even whole cells.
>
> [0014] In a biological application, the sol gel process comprises the preparation of an insoluble framework or cage in which the biological entity is entrapped or encapsulated."

This has nothing to do with forming nanoparticles which encapsulate biomolecules, not mentioning forming spherical nanoparticles with a diameter in a certain range.

The examiner respectfully reminds the Applicants that according to MPEP §2163:

> "**2163.02. Standard for Determining Compliance with Written Description Requirement**:
>
> The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the

art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

The Applicants did not show "possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention."

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6-21 and 23-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "wherein the nanoparticle is derived from a sol-gel". Sol-gel comprises a great variety of different materials, which makes it unclear, which material the nanoparticle is made of. Is this a metal nanoparticle? Is this something else? The Applicants are respectfully referred to the following excerpt from MPEP:

"§2171 **Two Separate Requirements for Claims Under 35 U.S.C. 112, Second Paragraph:**

The second paragraph of 35 U.S.C. 112 is directed to requirements for the claims:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

There are two separate requirements set forth in this paragraph:

(A) the claims must set forth the subject matter that applicants regard as their invention; and

(B) the claims must particularly point out and distinctly define the metes and

bounds of the subject matter that will be protected by the patent grant.

The first requirement is a subjective one because it is dependent on what the applicants for a patent regard as their invention. The second requirement is an objective one because it is not dependent on the views of applicant or any particular individual, but is evaluated in the context of whether the claim is definite - i.e., whether the scope of the claim is clear to a hypothetical person possessing the ordinary level of skill in the pertinent art.

Although an essential purpose of the examination process is to determine whether or not the claims define an invention that is both novel and nonobvious over the prior art, another essential purpose of patent examination is to determine whether or not the claims are precise, clear, correct, and unambiguous. The uncertainties of claim scope should be removed, as much as possible, during the examination process.

The inquiry during examination is patentability of the invention as applicant regards it. If the claims do not particularly point out and distinctly claim that which applicants regard as their invention, the appropriate action by the examiner is to reject the claims under 35 U.S.C. 112, second paragraph. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). If a rejection is based on 35 U.S.C. 112, second paragraph, the examiner should further explain whether the rejection is based on indefiniteness or on the failure to claim what applicants regard as their invention. *Ex parte Ionescu*, 222 USPQ 537, 539 Bd. App. 1984)"

Furthermore:

"§2172 **Subject Matter Which Applicants Regard as Their Invention:**

If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate. See *Morton Int 'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993)."

In the instant case "the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement".

Further, it is not clear, what the term "based on" refers to. Does it refer to the process of encapsulating the fluorescent material? It is not clear, how the process of entrapment of the protein-dye conjugate occurs, since in the sol-gel process the dye is entrapped in the matrix, rather than the particle.

Claim 7 is supposed to recite the limitation for the dye from claim 1; however, instead it recites the conjugate of the dye with the protein. Correction is required.

From claim 8 it is not clear, how the nanoparticle is modified, since it is totally unapparent, which material the nanoparticle is made of.

From claim 9 it is not clear, how the subject matter of the claim further limits the material of the nanoparticle.

Since claim 10 does not positively recite hydrophobic coating, it is not apparent, how claim 10 further limits the structure of the nanoparticle.

From claim 12 it is not clear, what does it mean "high fluorescence intensity", since "high" is a relative term.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. **Claims 1, 6, 12, 18 and 19** are rejected under 35 U.S.C. 103(a) as being unpatentable over Muller-Shutle (US 2005/0147974, IDS) in view of Senarath-Yapa et al. (Anal. Chimica Acta, 2001) (Senarath-Yapa).

Regarding *Claims 1, 6 and 12* Muller-Shutle discloses 500 nm -10 μm (par. [0051]) spherical nanoparticles made of silica gel and encapsulating a dye.

He does not specifically disclose the dye conjugated with a biomolecule, such as protein or DNA or silica such s TMOS.

Senarath-Yapa discloses preventing leaching of dye molecules from hydrated monoliths prepared from tetramethylorthosilicate (TMOS) by conjugating the dye with dendrimer or protein, e.g. myoglobin (Conclusion, p. 93, left column).

It would have been obvious for a person of ordinary skill in the art to modify Muller-Shutle's nanoparticles by binding dyes with biomacromolecules, such as proteins, in order to prevent the leaching of the dye from the TMOS nanoparticles.

Regarding claims 18 and 19 aminopropyloxysilane-derived sol-gel and tetramethyloxysilan gel are other types of silica gel, which are conventionally used for encapsulating dyes.

12. **Claims 7 and 11** are rejected under 35 U.S.C. 103(a) as being unpatentable over Muller-Shutle in view of Senarath-Yapa, as applied to claims 1, 6, 12, 18 and 19 above, and further in view of Theaker and Rowell (Analyst, 2003).

Muller-Shutle in view of Senarath-Yapa do not specifically disclose dye-protein conjugates as fluorescence materials in the nanoparticles. Theaker and Rowell disclose Texas Red-gelatin conjugate immobilized in the sol-gel matrix as fluorescence materials. It would have been obvious for a person of ordinary skill in the art to use Texas Red-gelatin conjugate instead of dye-dendrimer or dye-moyglobin conjugates encapsulated in the silica-gel nanoparticles of Muller-Shutle and Senarath-Yapa in order to use them for e.g. fluorometric analysis. Texas Red-porcine thyroglobluin conjugate is an obvious variant of another conjugate with Texas Red which can be used for fluorometric analysis.

13. **Claims 8-10, 13-17 and 23-26** are rejected under 35 U.S.C. 103(a) as being unpatentable over Muller-Shutle in view of Senarath-Yapa, as applied to claims 1, 6, 12, 18 and 19 above, and further in view of Turnell et al. (US 2006/0177416) (Turnell).

Muller-Shutle in view of Senarath-Yapa do not specifically disclose hydrophobic, i.e. lipophilic coating of the particles, specifically coating with surfactants such as phosphatidylcholine, or hydrophilic ionized coating, including polysilane.

Turnell discloses the following:

> "As illustrated in FIG. 2, a variety of bioactive agents, coating molecules and ligands for bioactive agents can be attached, for example covalently, to the surface of the polymer particles. Bioactive agents, such as targeting antibodies, polypeptides (e.g., antigens) and drugs, and the like, can be covalently conjugated to the surface of the polymer particles. In addition, coating molecules, such as polyethylene glycol (PEG) as a ligand for attachment of antibodies or polypeptides or phosphatidylcholine (PC) as a means of blocking attachment sites on the surface of the particles to prevent the particles from sticking to non-target biological molecules and surfaces in the patient may also be surface-conjugated (FIG. 3)."

It would have been obvious for a person of ordinary skill in the art to modify the surface of Muller-Shutle/Senarath-Yapa's nanoparticles the way it is disclosed by Turnell for the same purpose as disclosed by Turnell, or for specific binding with specific analytes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571)272-1257. The examiner can normally be reached on 9:30am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on 571-272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Yelena G. Gakh, Ph.D./
Primary Examiner, Art Unit 1777

12/12/2011

9. **Claims 1, 6 and 12** are rejected under 35 U.S.C. 102(e) as being anticipated by

The groups of inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the common technical feature of the groups is the nanoparticle recited in claim 1. Such nanoparicles are disclosed by e.g. *Goldmen et al.* in the paper "Conjugation of Luminescent Quantum Dots with Antibodies Using an Engineered Adaptor Protein to Provide New Reagents for Fluoroimmunoassays" (Anal. Chem., 2002).